Light and Life

Oh Agni! May you become alike the Sun and bless us with food grains.

Samaveda 1500-1000 BC



- Photomedicine
- Lithography
- => Industrial Synthesis of Chemicals
- Photography, Xeorography and Holography
- => TiO₂: Environmental Cleanup
- Solar Energy Conversion
- Sunsscreen, Photochromic Glass
- Photostabilization
- Photocuring



Biological Applications of Photochemistry

Photomedicine

Phototherapy - Jaundice Treatment

* PUVA therapy - Skin Disorders, Blood Cancer

Photodynamic therapy - Cancer

Lasik surgery - Vision Correction

Phototherapy for Neonatal Jaundice Treatment

- Accumulation of the potentially toxic yellow liphophilic bilirubin in human serum leads to Jaundice.
- If the percentage of bilirubin increases to 15-25 mg/100 ml, it will lead to hyperbilirubinemia.
- Severe hyperbilirubinemia cases, sufficient pigment may partition into the brain to cause irreversible damage, even death.



McDonagh etal., Science, 208, 1980, 145-151.

Biosynthesis of bilirubin



Glucuronyl transferase activity in fetal and new born liver is very low.

Why bilirubin is lipophilic (hydrophobic)?



Different ways to cure jaundice

- □ Wait till liver matures soon enough to clear bilirubin unaided.
- Exchange transfusion: blood along with threatening pigment drained and replaced with clean blood.
- **D** Phototherapy irradiate the baby with light.

Discovery of phototherapy

The discovery of phototherapy stems from the observations of Sister J. Ward, a nurse in U.K.

Evening walk with hyperbilirubinemia patients - lead to discovery of phototherapy by scientists.

" light converts bilirubin to a less hydrogen bonded (more water soluble) isomer"



Skin Disorders and PUVA therapy



Psoriasis



Polymorphic light eruption



Vitiligo - pigment cells are destroyed.



Acute dermatitis

PUVA- therapy

- **Egyptians and Asian Indians practised this therapy centuries ago.**
- Boiled extracts of fruits of plants *Ammi majus* in Egypt and *Psoralea Corylifolia* L in India plus sunlight cured vitiligo.
- In 1988, PUVA was the first FDA (Food and Drug Administration) approved selective immunotherapy for skin disorders including cancer.

Psoralen + UVA = PUVA therapy



How PUVA therapy is done ?

- Methoxsalen capsules are taken two hours before exposure to UVA.
- Bath PUVA: hands and/or feet are soaked in a dilute solution of methoxsalen for 30 minutes, then exposed to UVA.
- A few patients may be treated with topical tripsor
 PUVA a lotion is applied on the affected areas 10
 minutes before UVA exposure.

Photoadduct representation with DNA



• Intercalation

- Monofunctional adduct (3, 4 with pyrimidine base)
- Bifunctional crosslinked adduct(3, 4 and 4', 5' with pyrimidine bases)

PUVA -therapy to treat cancer

Centrifugation.

Separate white blood cells.

Drug in saline + Leukocytes.

Irradiate in the machine.

Collect white blood cells.



How a single treatment can activate the immune system in the protection against a dangerous cancer and suppress T cell activity in autoreactive disorders ?



Givardi etal., Annals of the New York Acad. Sciences, 941, 2001,1-17

Photodynamic therapy

- **Photodynamic therapy first used in 1978.**
- □ There is currently one photodynamic drug available on the market: Photofrin.[™]
- □ Approved for the treatment of esophageal and lung cancers.



Chlorins

Phthalocyanines





How does photodynamic therapy work?

- PDT requires sensitizer, light and oxygen in the target tissue.
- □ Light generates reactive oxygen species.
- Reactive oxygen species can kill targeted cells either by necrotic mechanisms or by initiating the apoptotic cascade.





Ideal wavelength 650nm



Many tumours have higher lipid content than normal cells, facilitating the uptake of lipophilic compounds such as photosensitizers.

MacRobert A. J et al., Chemistry and Industry, 1992, 17-20.

ALA (5-amino levulinic acid) - PDT

In 1999, FDA approved ALA-PDT for the treatment of actinic keratoses.



Levulan Process **Normal Process** Controlled synthesis of 5-ALA through Exogenous 5-ALA bypasses feedback mechanism and results in the feedback inhibition of the enzyme. accumulation of PpIX Glycine & Succinyl-CoA Glycine & Succinyl-CoA ALA-Synthase ALA-Synthase Topical or 5-ALA systemic 5-ALA 5-ALA administartion PBG PBG **PBG-Deaminase PBG-Deaminase** PpIX **PpIX** Ferrochelatse Ferrochelatse Heme Present in lesser amounts in Heme cancer cells



Current PDT applications in dermatology

- □ Actinic keratoses: Clinical response of 80%-100%.
- Squamous cell carcinoma: Clinical response 67-92%.
 100% curable at early stage.
- □ Basal cell carcinoma: 100% curable even in advanced stages.
- Mycosis fungoides-cutaneous cancer: ALA application was successfully used.

Photoablation and Lasik Surgery



R. Srinivasan



J. Wyne

Discovery in 1981 US FDA approval in 1995 Inducted into US Inventors Hall of Fame in 2002

Anatomy of Eye



 Light must be focused precisely on the retina for one to see an image clearly.

The light is focused by the eye through a process called refraction.

Refractive Errors

Myopia (Nearsighted) Hyperopia (Farsighted) Astigmatism

Photoablation with Excimer Lasers

Short wavelengths of light (190 to 300 nm) breaks molecular bonds (ablation)

Photablation with eximer laser (eg: ArF, KrF) can be done with a micron accuracy.

Refractive surgeries

PRK – Photorefractive keratotomy

LASIK – Laser assisted insitu keratomileusis



Histological photo of Rabbit cornea immediately following laser treatment.



Computer simulation of photoablation showing the movement of PMMA monomers as a function of time. Reproduced from Garrison and Srinivasan (1985) by permission. © 1985 American Institute of Physics

Photorefractive Keratectomy

- Cornea reshaped precisely with excimer laser, treatment is given on the corneal surface
- PRK works for myopia, hyperopia and astigmatism but not for astigmatism with hyperopia
- □ Healing time is relatively longer
- Used for people whose cornea epithelium is too thin to create a flap



How LASIK differs from PRK?

- □ LASER In-situ keratomilieusis (LASIK)
 - **First step is the lifting of corneal flap and then ablation**
 - **Treatment is given beneath the flap**



- □ Brief recovery time
- Very low infection risk and low enhancement rate
- Very low risk of scarring and minimal discomfort

Applications of Photolithography



Arunkumar Natarajan

Photolithography: First Invention 1949-50



Kodak's Louis Minsk Invents Negative Photoressist Polyvinylcinnamate



Kalle Company's (today Celanese) Otto Suess Invents Diazoquinone Based Positive Photoressist



Louis Plambeck

DuPont's Louis C. Plambeck Invents Photoinitiated, Acrylate-Based Photopolymer Relief Imaging

Photoresist

Photoresist

• Undergoes a chemical reaction <u>only</u> upon exposure to light.

Principle

• Create a difference between light exposed and unexposed regions

Types of photoresist

- Positive unexposed regions are retained
- Negative resist –exposed regions are retained



Two Types of Resists

Positive Photoresist



<u>Applications of the Principles of Photoresists and Lithography</u> *The Workhorses of Electronics and Printing*

- Printing, Litho, Package, Billboards
- Color Printing
- Printed Circuit Boards (PC)
- Integrated Circuit Chips (IC)
- Photopatterning-DNA and Biochips
- Micromachines

<u>Lithography Principles</u> *Imagewise Polymerization - Analog or Digital*

Lithographic Printing Is the **Backbone of Modern Printing** Industry

DUPONT PROGRESS REPORT

MARCH 33, 1958

No. 2a Mid-Atlantic Edition

DU PONT DISPLAYS PLATE AT NEWSPAPER CONFERENCE

MUMINGTON, DEL

Photomilal plates for ratery and flat bed use

Plans Three Types of Photopolymer Plates

PITTSBURGH, Pa., Mar. 13 - The Photo Products Department of E. I. du Pont de Nemours & Co., Inc., exhibited samples of experimental photopolymer printexhibited assumption of experimential protoprovision particu-ing plates induct to the reward in induct paper production mon attending to 8 Mid-Autonic Newspace Construction and Conference. These plates are composed a layer of photomensitive platic a layer of photomensitive platic a layer of photomensitive platic

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Printing Development

WILMINGTON, Del.

plane are to market three types of plates - a steel-supported plate about .060 inch thick with .030 inch relied; a steel-Laboratory Established

Gray Shading

-Mask -Resist Substrate

П

pp

ps

Three Color Printing

Color Printing Requires Color Separation

Color Printing is Done Through Four Color Processing

Printed Circuit Board Making

From Sand to Computer Chips

Photo Patterning-DNA Chip

Biosensors Based on Photopatterning

Optical micrograph of an array of cells formed using microcontact printing.

Polyethylene glycol polymer arrays formed using mid-UV photolithography.

Applications

- blood glucose measurements for diabetes management
- testing food for the presence of pathogenic
 microorganisms (*Salmonella* and *E. coli*)
- □ sensing chemical and biological warfare agents

Photochemical synthesis of Rose oxide Photochemical synthesis of Vitamin – D Photooximation - Synthesis of caprolactam Photochlorination

Rose oxide

(4r,2s)-(-)-cis-roseoxide

floral green with clean sharp, light, rose green note, diffusive, strong (Matsuda); also has been described as powerful fruity.

Odor Threshold = 0.5 ppb

(4s,2r)-(+)-cis-roseoxide

herbal, green floral, hay green, earthy, heavy (Matsuda); also has been described as sweet, floral

Odor Threshold = 50 ppb

Photograph of the cylindrical immersion type reactors used by Dragoco for the production of (-)-rose oxide

The reactor is about 3m tall, and is equipped with åa 5 k W light source.

Scanned from Photochemical technology, Braun, A. M., Maurette, M-. T., Oliveros, E.

Vitamin D is absolutely necessary for the efficient absorption of calcium and phosphate from our diet

Without vitamin D, the calcium passes through the digestive system unused.

Vitamin D is essential for the body's absorption of calcium.

Exactly how vitamin D controls our mineral metabolism is unknown.

However, there are three classical target tissues for its biological actions:

- a) intestine
- b) bone
- c) kidney

http://www.vitamind.com/whyimportant.htm

vitamin D₂ (ergocalciferol: plant origin) vitamin D₃ (cholecalciferol: animal origin).

Vitamin D crystals

Commercially synthesized by Roche-Vitamins

Commercial production of viatamin D_{3:}

a) 7-dehydrocholesterol

Extracted from animal skins (cow, pig or sheep) followed by an extensive purification.

b) cholesterol.

Extracted from the lanolin of sheep wool and can be converted to 7-dehydrocholesterol.

At the present time almost all milk sold commercially in the United States has 400 IU of chemically synthesized vitamin D_3 added per quart.

The ring opening take place from the first excited singlet state

Heat, moderate temperature

Vitamin D

(Se (Se Tachysterol (Tch)	ens. 0.15) ens. 0.58)	Image: wide wide wide wide wide wide wide wide
Sensitizer	E _T KJ Mol ⁻¹	(P-D/Tch)
Benzopheonone	286.3	2.6
Anthraquinone	260.8	2.1
2-Naphthylphenylketone	247.8	1.5
Benzil	22.5	1.8
9-Fluorenone	222.8	4.4
Benzanthrone	196.5	5.6
7,12-Dimethylbenzanhracene	185.2	16.3

Initial ratio (P-D/Tch)= 0.5; solvent=ethyl ether.

Photo-oximation

Photo-oximation is a special case of photo-nitrosylation.

Accidentally discovered by Lynn in 1919.

Important use in industrial application.

Photo-oximation of cyclohexane - industrial synthesis of *caprolactam*

Photo-oximation of cyclododecane – industrial synthesis of *lauryllactam*

Photochemical technology, Braun, A. M., Maurette, M-. T., Oliveros, E.

Tessenderlo's chemicals platform in Limburg, Belgium.

Investment, totals ~ FRF 170 million

Photochlorination

The new photochlorination plant will also produce

a) 15,000 tonnes of benzyl chloride and benzylidene chloride.

b) 7,000 tonnes of benzaldehyde.

These are some new addition to its range of synthetic organic products.

New chlorinated toluene derivatives production unit, Capacity > 60,000tonnes a year

http://www.groupe-emc.com/Portail/UK/actualites/actuUS1999-02.htm

- Photomedicine
- Lithography
- Industrial Synthesis of Chemicals
- Photography, Xeorography and Holography
- => TiO₂: Environmental Cleanup
- Solar Energy Conversion
- Sunscreen, Photochromic Glass
- Photostabilization
- ➡> Photocuring

"The rising sun is the giver of energy, heat, all powers, happiness and prosperity."

Rigveda 2000-1500 BC

